REMARKS

FORMAL MATTERS:

Claims 1, 3, 6-16, 18, and 21-34 are pending in the application after entry of the amendments set forth herein.

Claims 2, 4-5, 17 and 19-20 have been cancelled without prejudice.

Claims 1, 16, and 31 have been amended. Support for these amendments is found in the claims as originally filed and throughout the specification at, for example, Paragraph [0066] of the publication.

Accordingly, no new matter has been added.

REJECTIONS UNDER 35 U.S.C. § 103(A)

Claims 1, 3, 6-11, 29, 31, 32, and 34-Say, Mizutani, Saby

Claims 1, 3, 6-11, 29, 31, 32, and 34 were rejected under 35 U.S.C. §103(a) as being unpatentable over Say et al. (US Patent No. 6,103,033) in view of Mizutani et al. (Bull. Chem. Soc. Jpn., 64, 1991, pp. 2849-2851) and/or Saby et al. (Analytica Chemica Acta, 304, 1995, pp 33-39).

In making the rejection, the Examiner admits that Say does not explicitly disclose the use of a polymer that provides a hydrophilic domain. The Examiner then cites Mizutani to resolve this deficiency, alleging that Mizutani teaches combining the enzyme with a polymer such as polyethylene glycol (PEG) to improve the activity of the enzyme. The Examiner also cites Saby for teaching that PEG prevents the enzyme from denaturing in the carbon electrode.

In order to meet its burden in establishing a rejection under 35 U.S.C. § 103(a), the Office must first demonstrate that the combined prior art references teach or suggest all the claimed limitations. *See Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342 (Fed. Cir. 2007) ("the burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make [every element of] the composition or device, or carry out the [entire] claimed process, and would have had a reasonable expectation of success in doing so," (citing KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385, 1395 (U.S. 2007))).

Mizutani and/or Saby teach away from combination with Say.

It is the Applicant's position that the combination of Say, Mizutani, and Saby do not teach (as explained in the following section) all the claim limitations. However, even if Say were to be combined with Mizutani and/or Saby, Applicants submit that Mizutani and/or Saby actually teach away from a combination with Say.

In making this rejection, the Examiner asserts that "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention was made to utilize the teaching of either Mizutani and/or Saby for the biosensor of Say so as to improve the activity of the enzyme in the conductive ink by allowing it to better dissolve into or to prevent it from denaturing in the carbon based ink of Say." However, Applicants submit that the Examiner has not considered the entirety of the cited references.

According to MPEP §2143.03, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.,* 721 F. 2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert denied, 469 U.S> 851 (1984)." Furthermore, MPEP §2146 states that "[i]t is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F. 2d 731, 743, 218 USPQ 769, 779 (Fed. Cir, 1983)."

One of ordinary skill in the art would not be motivated to combine Say with Mizutani and/or Saby because the disclosures teach away from using the enzyme of Mizutani and Saby with the biosensor of Say. Mizutani and Saby disclose a modified enzyme in a carbon paste electrode. Also, the electrode in Say can be carbon based.

Then, Say teaches that the catalyst be preferably **non-leachably disposed on the sensor**. Say at column 19 discloses:

> Preferably, the catalyst is non-leachably disposed on the sensor, whether the catalyst is part of a solid sensing layer in the sensor or solvated in a fluid within the sensing layer. More preferably, the catalyst is immobilized within the sensor (e.g., on the electrode and/or within or between a membrane or film) to prevent unwanted leaching of the catalyst away from the working electrode **58** and into the patient. This may be accomplished, for example, by attaching the catalyst to a polymer, cross linking the catalyst with another electron transfer agent (which, as described above, can be polymeric), and/or providing one or more barrier membranes or films with pore sizes smaller than the catalyst.

On the other hand, Mizutani and Saby disclose that the carbon paste electrode comprising the PEG-modified glucose oxidase **leaches out of the carbon paste**. Page 2850 of Mizutani discloses the following, where CPE I is a carbon paste electrode having PEG-modified glucose oxidase:

> The effect of storage (in the acetate buffer at 0 °C) of CPE I and II was then examined. On each electrode, the response to glucose (25 mmol dm^{-3}) gradually decreased during storage and became ca. 80% of the initial value after 10 d; the long-term stability was, unfortunately, not improved by a modification of enzyme. The decrease in the electrode response was considered to be caused by a leaching of the (modified or native) enzyme out of the carbon paste matrix, since the solution used for storing CPE I or II showed significant GOD activity.

Page 38 of Saby discloses:

> Then, for these mediators, the lost of current response can be linked to the leakage of the PEG-modified GOD from the carbon paste.

Thus, while Say teaches use of a catalyst that is non-leachably disposed on the sensor, Mizutani and Saby teach use of a PEG-modified glucose oxidase that can leach out of a carbon paste electrode. If the PEG-modified glucose oxidase of Mizutani and Saby were used in the biosensor of Say, the enzyme would leach out of the sensor and the sensor would be inoperable. This result is already shown in Mizutani and Saby. Thus, one of ordinary skill in the art would be taught away from using the PEG-modified enzyme of Mizutani and Saby in the biosensor of Say.

Accordingly, there is no motivation or suggestion to combine Say, Mizutani, and Saby. For this reason alone, the rejection of Claims 1, 3, 6-11, 29, 31, 32, and 34 were rejected under 35 U.S.C. § 103(a) should be withdrawn.

Proposed modification to Say with Mizutani and/or Saby would render prior art invention unsatisfactory for its intended use.

Also, even if Say were to be combined with Mizutani and/or Saby, Applicants submit that the proposed modification to Say with Mizutani and/or Saby would render prior art invention unsatisfactory for its intended use.

According to MPEP §2143.01 which cites *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984), "[i]f proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification."

The manufacturing process of Say may not be compatible with the enzyme material of Mizutani and/or Saby. Say discloses a process for producing an electrochemical biosensor which contains crosslinked polymers. In column 31, Say discloses that a process for manufacturing a biosensor that includes a heating step when a sensor is deposited on the web. Column 31, lines 39-42 of Say discloses that

> The heating chamber **220** can also heat the web **202** to sufficient temperatures to cause potential polymerization reactions such as cross link reactions between polymers and the redox mediator and/or redox enzyme.

Thus, in the process of Say, the enzyme must be able to survive the heating steps and not all enzymes are compatible with the heating process of Say. Some enzymes can become denatured upon heating. If one of ordinary skill in the art were to subject the enzyme of Mizutani and Saby to the production process of Say, the resulting sensor would be inoperable because of denaturation of the enzyme.

The enzyme of Say is not the same nor can be reasonable compared to the enzyme of Mizutani and/or Saby. As discussed above, in Say, the enzyme is non-leachably disposed on the sensor. Say further discloses that the catalyst can be immobilized within the sensor. Mizutani and Saby disclose a PEG-modified glucose oxidase that is known to leach out of a carbon paste. From this characteristic, one of ordinary skill in the art would not consider the enzyme of Say to be the same or reasonable comparable to the enzyme of Mizutani and/or Saby. As a result, one of ordinary skill in the art would not want to subject the enzyme of Mizutani and/or Saby to the

heating steps taught and suggested by Say. Accordingly, there is no motivation to modify or replace the enzyme in process of Say and there is no *prima facie* case of obviousness.

Say, Mizutani, and Saby do not teach or suggest all the claim limitations.

As mentioned above, Applicants submit that not all the claim limitations are taught or suggested by the cited art. As amended, Claims 1, 16, and 31 recite, *inter alia*, "wherein the conductive ink comprises at least one enzyme, at least one mediator, and **a non-reactive component comprises** a polymer that provides hydrophilic domains in the conductive ink." Thus, the polymer with hydrophilic domains is a separate component from the other components in the conductive ink. None of Say, Mizutani, and Saby teach or suggest a conductive ink that comprises a polymer with hydrophilic domains that is a separate component from the other components.

As mentioned above, the Examiner admits that Say does not explicitly disclose the use of a polymer that provides a hydrophilic domain. Thus, Say does not teach or suggest a conductive ink that comprises a polymer with hydrophilic domains that is a separate component from the other components, as recited in the present claims.

Mizutani and Saby also do not teach or suggest a conductive ink that comprises a polymer with hydrophilic domains that is a separate component from the other components. In the experimental section, Mizutani teaches that an enzyme can be **modified** by exposing it to activated PEG, incubating the reaction for two hours at 37°C, stopping the reaction, removing any unattached PEG via ultrafiltration, and then using the **modified** enzyme in a carbon paste electrode. At page 34, Saby refers to this same technique and refers to the findings of Mizutani, stating that denaturation of the enzyme in the carbon electrode can be prevented by **modifying the enzyme with a polymer.** In Mizutani and Saby, the enzyme and PEG are attached to each other through the modification reaction.

Modified enzymes of Mizutani and Saby are not equivalent to claimed composition.

Modifying an enzyme via the teachings of Mizutani and Saby is not equivalent to incorporating PEG as a separate component into the conductive ink of an electrode, as in the claimed compositions.

The claimed compositions incorporate PEG directly into the ink as a non-reactive component and, thus, providing hydrophilic domains. On the other hand, Mizutani and Saby

utilize a **modified** enzyme in the conductive ink layer. The Applicants respectfully assert that including PEG as a component of the conductive ink of an electrode is not equivalent to modifying an enzyme with PEG and then incorporating that modified enzyme into the conductive ink of an electrode. The physical properties of an enzyme modified with PEG compared to a composition of an enzyme and PEG separate from each other are not the same. In fact, one of ordinary skill in the art would recognize that PEG modification can alter the properties of an enzyme. Thus, the modified enzymes of Mizutani and Saby are not equivalent to claimed composition.

The Applicants therefore assert that the Office has failed to meet its burden of demonstrating that the combined prior art references teach or suggest all the claimed limitations, thus failing to establish a *prima facie* case of obviousness.

Thus, Say et al. in view of Mizutani et al. and/or Saby et al. does not render obvious the presently claimed invention and the rejection of Claims 1, 3, 6-11, 29, 31, 32, and 34 under 35 U.S.C. §103(a) over Say et al. in view of Mizutani et al. and/or Saby et al. may be withdrawn.

Claims 1, 3, 6-11, 29, and 31-Say and Charlton

Claims 1, 3, 6-11, 29, and 31 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Say et al. (US Patent No. 6,103,033) in view of Charlton et al. (US Patent No. 5,798,031). This rejection was reiterated from the previous office action mailed October 2, 2008.

In making this rejection, the Examiner asserts that "Say does not explicitly disclose the use of a polymer that provides a hydrophilic domain. Charlton discloses that the enzyme can be deposited down onto an electrode in presence of a hydrophilic polymer, which would increase hydration access to the enzyme itself."

It is the Applicant's position that Charlton does not teach incorporation of the hydrophilic polymer in the conductive ink of the working electrode. As such, the combination does not teach each and every element found in the claims as required to establish a *prima facie* case of obviousness. However, in response, the Examiner asserts that the following:

> If it would have been obvious to add a hydrophilic polymer to the sensing layer of a sensor to improve the hydration of sample (as Charlton does suggest), then it would follow that it would have been obvious to add this same polymer to the conductive ink when the conductive ink contains the sensing layer components as well because the addition of the hydrophilic polymer ensures that the enzyme in the conductive ink would also be suitably hydrated with blood sample.

Applicants respectfully disagree. Addition of electrically conductive components to an electrode will affect the function of the electrode. As stated in Skoog et al. in the attached Appendix A, "it is useful to think of the cell reaction of an electrochemical cell as being made up of two half-cell reactions, each of which has a characteristic electrode potential associated with it." The electrode potential depends, in part, on the substance used to make the electrode. In Appendix A, a table from Skoog et al. is shown that includes a few electrode potentials. The table shows that different materials have different electrode potentials. Thus, if this concept is understood, one of ordinary skill in the art would not be motivated to incorporate additional elements in the conductive ink as different substances in the ink could affect the electrode potential in different ways.

In making the rejection, the Examiner also states:

> Because Say recognized that a number of non-conductive agents can be added to a conductive ink without destroying its sensing properties, one possessing ordinary skill in the art would recognize that adding any additional non-conductive agent, which the examiner would note applicant only adds in a 1% amount in the present invention (p. 20, ll. 25-27), would not destroy the function of the electrode. Moreover, the examiner is confused by the argument that one possessing ordinary skill in the art would not anticipate that incorporating a hydrophilic polymer into a conductive ink would allow the hydrophilic polymer to maintain its properties while also allowing the conductive ink to maintain its properties.

The Examiner states that Say recognizes that a number of non-conductive agents can be added to a conductive ink without destroying its sensing properties. However, a hydrophilic polymer can be a conductive agent. As a result, addition of a hydrophilic polymer to a conductive material can affect the electrode potential of the conductive material (see for example Appendix A of Skoog et. al.).

While it is the Applicant's position that Charlton does not teach incorporation of the hydrophilic polymer in the conductive ink of the working electrode, the combination of Say and Charlton is also improper. Accordingly, Applicants respectfully request that this rejection be withdrawn since the combination of references fails to teach each and every element found in the claims.

Claims 1, 3, 6-16, 18, and 21-34-Feldman, Say, Mizutani, and Saby

Claims 1, 3, 6-16, 18, and 21-34 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Feldman in view of Say and either Mizutani and/or Saby.

As stated above, none of Say, Mizutani, and Saby teach or suggest a conductive ink that comprises a polymer that is a separate component from the other components.

The Examiner uses Feldman to teach a biosensor. Feldman does not teach or suggest a conductive ink that comprises a polymer that is a separate component from the other components. Thus, Feldman still does not correct the deficiencies of Say, Mizutani, and Saby nor provide suggestion or motivation for combining the references.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claims 1, 3, 6-16, 18, and 21-31-Feldman, Say, and Charlton

Claims 1, 3, 6-16, 18, and 21-31 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Feldman in view of Say and Charlton. This rejection was reiterated from the previous office action mailed October 2, 2008.

As noted in the previous Office Action, both Say and Feldman **do not teach incorporation of the hydrophilic polymer in the conductive ink of the working electrode**. The Office Action turns to Charlton et al for teaching of a hydrophilic polymer. However, the teaching of Charlton is limited to the deposition of the hydrophilic polymer in a reagent layer

over the surface of electrodes (see column 1, lines 45-60). Therefore, similar to Say and Feldman, **Charlton also does not teach incorporation** of the hydrophilic polymer in the conductive ink of the working electrode. **The only teaching of incorporation of the hydrophilic polymer in a conductive ink is found in the present application**.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claims 32 and 34- Say, Charlton, and Yamashita

Claims 32 and 34 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Say in view of Charlton, and in further view of Yamashita.

As stated above, it is the Applicant's position that Charlton does not teach incorporation of the hydrophilic polymer in the conductive ink of the working electrode.

Also, as stated above, the combination of Say and Charlton is improper. One of ordinary skill in the art would not be motivated to add a hydrophilic polymer of Say to the conductive ink of Charlton because the electrode potential would be affected.

The Examiner uses Yamashita to teach the use of the hydrophilic polymer polyethylene glycol. Thus, Yamashita still does not correct the deficiencies of Say and Charlton nor provide suggestion or motivation for combining the references.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claims 32-34- Feldman, Say, Charlton, and Yamashita

Claims 32-34 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Feldman in view of Say and Charlton, and in further view of Yamashita. This rejection was reiterated from the previous office action mailed October 2, 2008.

As noted above with respect to claims 1, 16 and 31, which claims 32-34 depend from, the combination of Feldman in view of Say and Charlton fails to teach incorporation of a hydrophilic polymer in the conductive ink of a sensor electrode. Yamashita has been cited for teaching the use of the hydrophilic polymer polyethylene glycol. However, Yamashita also fails to teach incorporation of a hydrophilic polymer in the conductive ink of a sensor electrode. Therefore, Yamashita fails to make up the deficiency of Feldman, Say and Charlton.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Office finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, reference number ADCI-073.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 15, 2009

By: /Edward J. Baba, Reg. No. 52,581/
Edward J. Baba
Registration No. 52,581

Date: June 15, 2009

By: /Connie C. Tong, Reg. No. 52,292/
Connie C. Tong
Registration No. 52,292

BOZICEVIC, FIELD & FRANCIS LLP
235 Montgomery St., 29th Floor
San Francisco, CA 94104
Telephone: (415) 230-8100
Facsimile: (415) 230-5131